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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/586,594	01/16/1996	JEFFREY M. FRIEDMAN	600-1-162	3635

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DAVID A JACKSON
KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/586,594	FRIEDMAN ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9 and 14-68* is/are pending in the application.

4a) Of the above claim(s) *6,14-62,64,65 and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,7, 8,63,66 and 68* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☒ Claim(s) *3-9 and 14-68* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/27/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 3-9 and 14-68 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group V, drawn to murine splice variant OB-Re polypeptide, and hybrid polypeptide splice variants of OB-Re, in Paper No. 20 is acknowledged. The traversal is on the ground(s) that even with patentably distinct inventions, restriction is not required unless one of the following reasons appear (MPEP 808.2): 1) separate classification, 2) separate status in the art; or 3) different field of search. Applicants additionally point out that under Patent Office examining procedures, "If the search and examination of an entire application can be made without serious burden, the Examiner is encouraged to examine it on the merits, even though it includes claims to distinct or independent inventions" (MPEP 803< Rev. 8, May 1988). Applicants also submit that particularly as the claims of the respective groups are the same, a search could be economically conducted for each of the interpretations of the claims without undue hardship, and this is particularly true in the case of claim Groups I-VI, as both the same claims are the same area of classification are specified.

This is not found persuasive because under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05 - § 806.05(I): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) - § 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. The splice variants of the different groups would require separate sequence searches, which would be a different field of search for each group. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of hybrid OB-Re receptor wherein the N-terminal sequence is amino acid residues 28-796 (SEQ ID NO: 87) and the C-terminal sequence is NO: 15 after His 796 (SEQ ID NO: 90), wherein the numbering is based on the amino acid sequence of SEQ ID NO: 55 in the Paper filed Oct. 27, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6, 14-62, 64, 65 and 67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 20.

Claims 3-5, 7-9, 63, 66 and 68 are currently under examination and will be examined as far as they relate to the OB-Re splice variant of SEQ ID NO: 10.

Specification

3.1 The disclosure is objected to because of the following informalities: on page 25, line 11, "JAC" should be "JAK".

Appropriate correction is required.

3.2 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: DB, The Receptor For LEPTIN.

Advisory Information

3. Claims 5 and 9 are being examined as they are drawn only to the protein of SEQ ID NO: 10. Claims 3-5, 7,8, 63, 66 and 68 are being examined as they are drawn to both the protein of SEQ ID NO: 10 and the hybrid (truncated) protein.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It was not executed in accordance with either 37 CFR 1.66 or 1.68. Applicants in a communication filed July 24, 1996, stated that two (2) combined Declaration and Power of Attorney forms making reference to the above-identified application, were submitted, however, only one Declaration and Power of Attorney form is present in the case in which Ricardo Proenca had signed the declaration. The signatures of the other two inventors are missing.

Claim Objections

5.1 Claims 3-5, 7-9 and 68 are objected to because of the following informalities: they encompass non-elected inventions, which should be deleted. Appropriate correction is required.

5.2 Claim 7 is objected to because it is not in sequence compliance. The elected invention of claim 7 encompasses a (hybrid) leptin (OB-Re) polypeptide wherein the N-terminal sequence is amino acid residues 28-796 (SEQ ID NO: 87) and the C-terminal sequence is NO: 15 after His 796 (SEQ ID NO: 90), wherein the numbering is based on the amino acid sequence of SEQ ID NO: 55. Claim 7 does not comply with 37 CFR j 1.822(e) which states that (a) sequence that is made up of one or more noncontiguous segments of a larger sequence or segments from different sequences shall be presented as a separate sequence". However, the elected hybrid leptin polypeptide is identical to the polypeptide of SEQ ID NO: 10, with the exception that it is lacking the first 27 amino acids of SEQ ID NO: 10. For clarity, it is recommended that the claim be amended to claim the hybrid as follows: "leptin receptor polypeptide consisting of amino acids 28-805 of SEQ ID NO: 10". Otherwise, a new CRF and sequence listing will be required that recite the elected hybrid by a separate SEQ ID NO:, and the claims and the instant specification would also need to be amended so that they comply with 37 C.F.R. j 1.821(d) which requires a reference to that particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

If applicants elect to claim the hybrid receptor this way, the specification would also need to be amended so that it identifies the hybrid in the same way. This would not constitute new matter.

5.3 Claim 68 is indefinite because claim X is an improper dependent claim; it recites "...leptin receptor of any of claims 3-9....", so the receptor could be from one, two or more of the claims. Multiple dependent claims must refer to the claims from which they depend in the

alternative only, not inclusively. It is suggested the claim be rewritten as: "The leptin receptor of any one of claims 3-5 or 7-9 which is a murine leptin." See M.P.E.P. 608.01(n) for acceptable multiple dependent claim wording.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 3-5, 7-9 and 68 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 3-5, 7-9 and 68, as written, do not sufficiently distinguish over leptin receptors as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7.1 Claim 66 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 66 encompasses a body appearance improving cosmetic composition for reducing the body weight of an individual comprising a soluble leptin receptor. However, a composition comprising a soluble leptin receptor, when administered to a subject, would not result in weight loss, but weight gain. Stimulation of the leptin receptor would result in weight loss, and inhibiting the stimulation of the leptin receptor (such as a soluble leptin receptor binding the ligand leptin and thereby inhibiting leptin and leptin receptor binding) would result in weight gain. See Tartaglia et al., US Patent No. 6,506,877, column 8, lines 44-49 and column 45, lines 8-67. Therefore, the claim is not enabled for a composition comprising a soluble leptin receptor that would result in weight

7.2 Claims 3-5, 7, 8, 63, 66 and 68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO: 55, which is the murine full-length leptin (OB) receptor, and a splice variant (SEQ ID NO: 10) that is a soluble form of the full-length receptor. The claims are directed to the splice variant, which is shown to have the following activity: binding leptin. However, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a full-length protein, that of SEQ ID NO: 55, and the splice variants, all of which are identical to at least amino acids 1-664 of SEQ ID NO: 55, which is the majority of the extracellular domain, does not adequately support the scope of the claimed

genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, an isolated polypeptide sequence SEQ ID NO: 55 and five splice variants. Receptor function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming

Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does not allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polypeptides encompassed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 8, 63, 66 and 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Tartaglia et al., US Patent No. 6,506,877, filing date Dec. 28, 1995.

Claims 8, 63, 66 and 68 encompass a leptin receptor (OB-R polypeptide) which is a soluble receptor, which may be a murine receptor, and pharmaceutical composition or body appearance improving cosmetic composition for reducing body weight comprising soluble leptin receptor and a pharmaceutically acceptable carrier.

Tartalgia et al. disclose human and murine Ob (leptin) receptors (see entire patent), wherein the receptors may be soluble (column 5, lines 32-34, column 8, lines 34-49, column 13, lines 17-19, column 17, lines 54-61, column 31, lines 5-12 for example), and pharmaceutical compositions or body appearance improving cosmetic compositions (column 46, line 1-column 47, line 58). Also, Tartaglia et al. discloses a protein (SEQ ID NO: 2) that is 100% identical to amino acids 1-796 of SEQ ID NO: 10 of the instant invention, which is the soluble portion of the protein. Therefore, Tartaglia et al. anticipates the claims.

Conclusion

9.1 3-5, 7, 8, 63, 66 and 68 are rejected.

9.2 Claim 9 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM. ***Applicant is advised that effective January 23, 2003, the Examiner's phone number will be (571) 272-0878.***

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564. ***Applicant is advised that effective January 23, 2003, Yvonne Eyler's phone number will be (571) 272-0871.***

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner